

PATENT COOPERATION TREATY

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Commissioner
US Department of Commerce
United States Patent and Trademark
Office, PCT
2011 South Clark Place Room
CP2/5C24
Arlington, VA 22202
ETATS-UNIS D'AMERIQUE
in its capacity as elected Office

| | |
|---|---|
| Date of mailing (day/month/year) 08 June 2001 (08.06.01) | |
| International application No. PCT/US00/23723 | Applicant's or agent's file reference WST89APCT |
| International filing date (day/month/year) 30 August 2000 (30.08.00) | Priority date (day/month/year) 31 August 1999 (31.08.99) |
| Applicant PRENDERGAST, George, C. et al | |

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:
21 March 2001 (21.03.01)

☐ in a notice effecting later election filed with the International Bureau on:

2. The election ☒ was
☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

| | |
|---|----------------------------------|
| The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland | Authorized officer Odile ALIU |
| Facsimile No.: (41-22) 740.14.35 | Telephone No.: (41-22) 338.83.38 |

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

REC'D 13 AUG 2001

PCT

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|--|--|--|
| Applicant's or agent's file reference WST89APCT | FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416) | |
| International application No. PCT/US00/25723 | International filing date (day/month/year) 30 AUGUST 2000 | Priority date (day/month/year) 31 AUGUST 1999 |
| International Patent Classification (IPC) or national classification and IPC Please See Supplemental Sheet. | | |
| Applicant THE WISTAR INSTITUTE OF ANATOMY AND BIOLOGY | | |

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 5 sheets.
☒ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority. (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).
 These annexes consist of a total of 5 sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☒ Non-establishment of report with regard to novelty, inventive step or industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability, citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☐ Certain observations on the international application

| | |
|--|--|
| Date of submission of the demand 21 MARCH 2001 | Date of completion of this report 17 MAY 2001 |
| Name and mailing address of the IPEA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 | Authorized officer TEKCHAND SAIDHA |
| Facsimile No. (703) 305-3230 | Telephone No. (703) 308-0196 |

I. Basis of the report1. With regard to the **elements** of the international application:*☐ the international application as originally filed☒ the description:

pages 1-39 , as originally filed
pages NONE , filed with the demand
pages NONE , filed with the letter of _____

☒ the claims:

pages NONE , as originally filed
pages NONE , as amended (together with any statement) under Article 19
pages 40-44 , filed with the demand
pages NONE , filed with the letter of _____

☒ the drawings:

pages 1-8 , as originally filed
pages NONE , filed with the demand
pages NONE , filed with the letter of _____

☒ the sequence listing part of the description:

pages NONE , as originally filed
pages NONE , filed with the demand
pages NONE , filed with the letter of _____

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language _____ which is:

☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).☐ the language of publication of the international application (under Rule 48.3(b)).☐ the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:☐ contained in the international application in printed form.☐ filed together with the international application in computer readable form.☐ furnished subsequently to this Authority in written form.☐ furnished subsequently to this Authority in computer readable form.☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.4. ☒ The amendments have resulted in the cancellation of:☒ the description, pages NONE☒ the claims, Nos. NONE☒ the drawings, sheets/fig NONE5. ☐ This report has been drawn as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

* Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).

**Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International Application No.

PCT/US00/23723

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been and will not be examined in respect of:

☐ the entire international application.

☒ claims Nos. 10-13, 15-21, 23-27

because:

☐ the said international application, or the said claim Nos. _ relate to the following subject matter which does not require international preliminary examination (*specify*).

☒ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. 10-12, 15, 17 & 20 are so unclear that no meaningful opinion could be formed (*specify*).

because they are multiple dependent claims and are not drafted in accordance with second and third sentences of rule 6.4(a).

☐ the claims, or said claims Nos. _ are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for said claims Nos. (See Attached).

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the standard.

☐ the computer readable form has not been furnished or does not comply with the standard.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

Intern application No.

PCT/US00/23723

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step r industrial applicability; citations and explanations supporting such statement**1. statement**

| | | |
|-------------------------------|---------------------------|-----|
| Novelty (N) | Claims <u>1-9, 14, 22</u> | YES |
| | Claims <u>NONE</u> | NO |
| Inventive Step (IS) | Claims <u>1-9, 14, 22</u> | YES |
| | Claims <u>NONE</u> | NO |
| Industrial Applicability (IA) | Claims <u>1-9, 14, 22</u> | YES |
| | Claims <u>NONE</u> | NO |

2. citations and explanations (Rule 70.7)

Claims 1-9, 14 & 22 meet the criteria set out in PCT Article 33(2)-(4), because the prior art does not teach or fairly suggest the Bin2 protein or the fragments specifically selected from the amino acids 1-137 or 179-336 or 250-564 of SEQ ID NO : 2. Prendergast et al. (US 5,605,830 A) teaches an amino acid sequence (SEQ ID NO : 4) residues 136-153, which match the Applicants' SEQ ID NO : 2, residues 138-155. However, the claimed residues are outside the range of teachings of Prendergast et al. Similarly the nucleic acid encoding the Bin2 protein, vector, host cell, reagent composition comprising Bin2 protein are structurally distinct.

Claims 1-9, 14 & 22 meet the criteria set out in PCT Article 33(3), because the subject matter claimed can be made or used in industry.

_____ NEW CITATIONS _____
NONE

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US00/23723

Supplemental Box

(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: Boxes I - VIII

Sheet 10

CLASSIFICATION:

The International Patent Classification (IPC) and/or the National classification are as listed below:
IPC(7): C12P 21/06; C07H 21/04; C12N 5/00, 1/20, 15/09, 15/63; A61K 38/00; C07K 1/00 and US Cl.: 435/69.1, 325, 252.3, 320.1; 536/23.1, 23.5; 530/300, 350

III. NON-ESTABLISHMENT OF REPORT:

No international search report has been established for claim numbers 13, 16, 18-19, 21, 23-27 .

WHAT IS CLAIMED IS:

1. A Bin2 protein having the amino acid sequence of SEQ ID NO:2.
2. A Bin2 peptide or protein selected from the group consisting of:
 - (a) a fragment of Bin2 comprising at least 8 amino acids in length, said fragment selected from the sequence of amino acids 1-137 of SEQ ID NO: 2, amino acids 179 to 336 of SEQ ID NO: 2; and amino acids 250 to 564 of SEQ ID NO: 2;
 - (b) a fragment of Bin2 comprising the sequence of amino acids 23 to 35 of SEQ ID NO:2 said fragment being at least 14 amino acids in length;
 - (c) an analog or homolog of SEQ ID NO:2;
 - (d) a fusion protein comprising the amino acid sequence of (a) to (c) and a fusion partner;
 - (e) a deletion protein comprising the amino acid sequence of SEQ ID NO:2 with one to twenty amino acids deleted therefrom.
3. The Bin2 peptide or protein according to claim 2, wherein the fragment of Bin2 has the sequence of amino acids 1 to 221 of SEQ ID NO:2.
4. The Bin2 peptide or protein according to claim 2, wherein the fragment of Bin2 is at least 8 amino acids in length and comprising a sequence of contiguous amino acids selected from the sequence of amino acids 1 to 13 of SEQ ID NO: 2.
5. The Bin2 peptide or protein according to claim 2, wherein the fusion partner is selected from the group consisting of glutathione-S-transferase, β -galactosidase, poly-histidine and maltose binding protein.

6. A Bin2 nucleic acid sequence encoding a protein of SEQ ID NO: 2 or peptide selected from the group consisting of:

(a) a fragment of Bin2 comprising at least 8 amino acids in length, said fragment selected from the sequence of amino acids 1-137 of SEQ ID NO: 2, amino acids 179 to 336 of SEQ ID NO: 2; and amino acids 250 to 564 of SEQ ID NO: 2;

(b) a fragment of Bin2 comprising the sequence of amino acids 23 to 35 of SEQ ID NO:2 said fragment being at least 14 amino acids in length;

(c) an analog or homolog of SEQ ID NO:2;

(d) a fusion protein comprising the amino acid sequence of (a) to (c) and a fusion partner;

(e) a deletion protein comprising the amino acid sequence of SEQ ID NO:2 with one to twenty amino acids deleted therefrom.

7. A nucleic acid sequence selected from the group consisting of:

(a) a nucleic acid sequence which hybridizes to the sequence of claim 1 under stringent conditions;

(b) a nucleic acid sequence complementary to the sequence of claim 1; and

(c) an allelic variant of any of (a) through (b).

8. A nucleic acid sequence encoding a fusion protein according to claim 2 or claim 5.

9. A vector comprising a nucleic acid sequence according to claim 6 under the control of regulatory sequences which direct expression of the Bin2 protein.

10. A vector comprising a nucleic acid sequence according to claims 7 or 8 said sequence under the control of regulatory sequences.

11. A host cell transformed with a vector according to claim 9 or 10.
12. A diagnostic reagent comprising a nucleic acid sequence of any of claims 6, 7, or 8 and a detectable label which is associated with said sequence.
13. A method for diagnosing hepatocarcinoma, said method comprising the steps of amplifying the DNA in a sample from a patient suspected of having hepatocarcinoma using a nucleic acid sequence according to claims 6 or 7.
14. A diagnostic reagent comprising a protein according to claim 1 or claim 2 and a detectable label which is associated with said protein.
15. A method for specifically diagnosing cancers associated with inappropriate expression of Bin1 comprising the steps of:
 contacting a sample from a human or animal to be diagnosed with the Bin2 protein of claim 1 or 2, or the diagnostic reagent of claim 12, whereby in the presence of Bin1 in the sample, a complex is formed between Bin1 and the Bin2 protein or reagent, and
 analyzing for the presence or quantity of said complex.
16. An isolated anti-Bin2 antibody which is specific for the protein of claim 1 or 2.
17. The anti-Bin2 antibody according to claim 16, isolated by immunizing said host with the protein of claim 1 or the protein of claim 2.
18. The anti-Bin2 antibody according to claim 16 which is selected from the group consisting of a chimeric antibody, a humanized antibody, a monoclonal antibody and a polyclonal antibody.

19. A diagnostic reagent comprising the anti-Bin2 antibody according to claim 18 and a detectable label.

20. A method of diagnosing cancer or hyperplastic disease characterized by inappropriate levels of functional Bin1 levels in a human or an animal, said method comprising the steps of:

contacting a Bin2 protein according to claim 1 or 2 or diagnostic reagent of claim 19 with a sample from a human or animal to be diagnosed, whereby in the presence of Bin1, a detectable complex is formed with the Bin2 protein or diagnostic reagent,

analyzing for the presence or absence of said complex; and

comparing the level of complex to a standard, wherein the absence of said detectable label indicates the absence of or decreased levels of functional Bin1.

21. A kit for diagnosing a condition associated with Bin2 comprising a diagnostic reagent according to claims 19.

22. A composition comprising an effective amount of a Bin2 protein of claim 1 or claim 2 and a pharmaceutically acceptable carrier.

23. A method of detecting inappropriate expression of bridging integrator protein-2 (Bin2) in a patient comprising providing a sample from a patient suspected of having said inappropriate expression; incubating said sample in the presence of a diagnostic reagent according to claim 19; and comparing levels of expression to a normal Bin2 control.

24. A method of detecting inappropriate expression of bridging integrator protein-2 (Bin 2) in a patient comprising providing a sample from a patient suspected of having said overexpression and performing nucleic acid amplification using the nucleic acid sequence according to claim 6 or claim 7.

25. A method of identifying compounds which specifically bind to Bin2, comprising the steps of contacting said Bin2 or a fragment thereof with a test compound to permit binding of the test compound to Bin2; and determining the amount of test compound which is bound to Bin2.

26. A method of identifying compounds which inhibit the binding of Bin2, comprising the steps of:

(a) contacting an amount of immobilized first Bin peptide or a fragment thereof with a test compound and an amount of labeled second Bin peptide or fragment, wherein said first Bin peptide is either a Bin1 or a Bin2 peptide, and the second Bin peptide is the Bin peptide that binds said first Bin peptide;

(b) separating unbound material from immobilized material of (a),
and

(c) measuring the amount of label on said immobilized material,
wherein a decrease in the amount of label immobilized in the presence of test compound compared to the amount of label immobilized in the presence of a control peptide or protein, indicates that said test compound inhibits the binding of Bin1 to Bin 2.

27. A compound identified by the method of claim 25 or 26.

The demand must be filed directly with the competent International Preliminary Examining Authority, or, if more than one Authority is competent, with the one chosen by the applicant. The full name or two-letter code of that Authority may be indicated by the applicant on the line below:

IPEA/ US



PATENT TRADEMARK OFFICE

PCT

CHAPTER II

DEMAND

under Article 31 of the Patent Cooperation Treaty:
The undersigned requests that the international application specified below be the subject of international preliminary examination according to the Patent Cooperation Treaty and hereby elects all eligible States (except where otherwise indicated).

| For International Preliminary Examining Authority use only | | |
|---|---|--|
| Identification of IPEA | | Date of receipt of DEMAND |
| Box No. I IDENTIFICATION OF THE INTERNATIONAL APPLICATION | | Applicant's or agent's file reference WST89APCT |
| International application No. PCT/US00/23723 | International filing date (day/month/year) 30 August 2000 (30.08.00) | (Earliest) Priority date (day/month/year) 31 August 1999 (31.08.99) |
| Title of invention BRIDGING INTEGRATOR-2 (BIN2) NUCLEIC ACID MOLECULES AND PROTEINS AND USES THEREFOR | | |
| Box No. II APPLICANT(S) | | |
| Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.) The Wistar Institute of Anatomy and Biology 3601 Spruce Street Philadelphia, Pennsylvania 19104 US | | Telephone No.: 215-898-0049 Facsimile No.: 215-573-2456 Teleprinter No.: |
| State (that is, country) of nationality: US | | State (that is, country) of residence: US |
| Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.) Prendergast, George C. 414 Bryn Mawr Avenue Bala-Cynwyd, Pennsylvania 19004 US | | |
| State (that is, country) of nationality: US | | State (that is, country) of residence: US |
| Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.) Ge, Kai 4427 Spruce Street Philadelphia, Pennsylvania 19104 US | | |
| State (that is, country) of nationality: China | | State (that is, country) of residence: US |
| <input type="checkbox"/> Further applicants are indicated on a continuation sheet. | | |

Box No. III AGENT OR COMMON REPRESENTATIVE; R ADDRESS FOR CORRESPONDENCE

The following person is ☒ agent ☐ common representative
 and ☒ has been appointed earlier and represents the applicant(s) also for international preliminary examination.
☐ is hereby appointed and any earlier appointment of (an) agent(s)/common representative is hereby revoked.
☐ is hereby appointed, specifically for the procedure before the International Preliminary Examining Authority, in addition to the agent(s)/common representative appointed earlier.

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)*

Bak, Mary E.
 Howson and Howson
 Spring House Corporate Center
 P.O. Box 457
 Spring House, Pennsylvania 19477
 US

Telephone No.:

215-540-9200

Facsimile No.:

215-540-5818

Teleprinter No.:

☐ Address for correspondence: Mark this check-box where no agent or common representative is/has been appointed and the space above is used instead to indicate a special address to which correspondence should be sent.

Box No. IV BASIS FOR INTERNATIONAL PRELIMINARY EXAMINATION**Statement concerning amendments:***

1. The applicant wishes the international preliminary examination to start on the basis of:

☐ the international application as originally filed

the description ☒ as originally filed

☐ as amended under Article 34

the claims ☐ as originally filed

☐ as amended under Article 19 (together with any accompanying statement)

☒ as amended under Article 34

the drawings ☒ as originally filed

☐ as amended under Article 34

2. ☐ The applicant wishes any amendment to the claims under Article 19 to be considered as reversed.

3. ☐ The applicant wishes the start of the international preliminary examination to be postponed until the expiration of 20 months from the priority date unless the International Preliminary Examining Authority receives a copy of any amendments made under Article 19 or a notice from the applicant that he does not wish to make such amendments (Rule 69.1(d)). *(This check-box may be marked only where the time limit under Article 19 has not yet expired.)*

* Where no check-box is marked, international preliminary examination will start on the basis of the international application as originally filed or, where a copy of amendments to the claims under Article 19 and/or amendments of the international application under Article 34 are received by the International Preliminary Examining Authority before it has begun to draw up a written opinion or the international preliminary examination report, as so amended.

Language for the purposes of international preliminary examination: English

☒ which is the language in which the international application was filed.

☐ which is the language of a translation furnished for the purposes of international search.

☐ which is the language of publication of the international application.

☐ which is the language of the translation (to be) furnished for the purposes of international preliminary examination.

Box No. V ELECTION OF STATES

The applicant hereby elects all eligible States *(that is, all States which have been designated and which are bound by Chapter II of the PCT)*

excluding the following States which the applicant wishes not to elect:

Box No. VI CHECK LIST

The demand is accompanied by the following elements, in the language referred to in Box No. IV, for the purposes of international preliminary examination:

- | | | | |
|--|---|---|--------|
| 1. translation of international application | : | | sheets |
| 2. amendments under Article 34 | : | 5 | sheets |
| 3. copy (or, where required, translation) of amendments under Article 19 | : | | sheets |
| 4. copy (or, where required, translation) of statement under Article 19 | : | | sheets |
| 5. letter | : | 2 | sheets |
| 6. other (specify) | : | | sheets |

For International Preliminary Examining Authority use only

received not received

| | |
|--------------------------|--------------------------|
| <input type="checkbox"/> | <input type="checkbox"/> |
| <input type="checkbox"/> | <input type="checkbox"/> |
| <input type="checkbox"/> | <input type="checkbox"/> |
| <input type="checkbox"/> | <input type="checkbox"/> |
| <input type="checkbox"/> | <input type="checkbox"/> |
| <input type="checkbox"/> | <input type="checkbox"/> |

The demand is also accompanied by the item(s) marked below:

- | | |
|--|---|
| 1. <input checked="" type="checkbox"/> fee calculation sheet | 4. <input type="checkbox"/> statement explaining lack of signature |
| 2. <input type="checkbox"/> separate signed power of attorney | 5. <input type="checkbox"/> nucleotide and or amino acid sequence listing in computer readable form |
| 3. <input type="checkbox"/> copy of general power of attorney; reference number, if any: | 6. <input type="checkbox"/> other (specify): |

Box No. VII SIGNATURE OF APPLICANT, AGENT OR COMMON REPRESENTATIVE

Next to each signature, indicate the name of the person signing and the capacity in which the person signs (if such capacity is not obvious from reading the demand).

By: Mary E. Bak
Mary E. Bak

For International Preliminary Examining Authority use only

1. Date of actual receipt of DEMAND:

2. Adjusted date of receipt of demand due to CORRECTIONS under Rule 60.1(b):

3. ☐ The date of receipt of the demand is AFTER the expiration of 19 months from the priority date and item 4 or 5, below, does not apply. ☐ The applicant has been informed accordingly.

4. ☐ The date of receipt of the demand is WITHIN the period of 19 months from the priority date as extended by virtue of Rule 80.5.

5. ☐ Although the date of receipt of the demand is after the expiration of 19 months from the priority date, the delay in arrival is EXCUSED pursuant to Rule 82.

For International Bureau use only

Demand received from IPEA on:

PCT

REQUEST

The undersigned requests that the present international application be processed according to the Patent Cooperation Treaty.



00270

For receiving Office use only
PATENT TRADEMARK OFFICE

International Application No.

International Filing Date

Name of receiving Office and "PCT International Application"

Applicant's or agent's file reference
(if desired) (12 characters maximum) WST89APCT

Box No. I TITLE OF INVENTION

BRIDGING INTEGRATOR-2 (BIN2) NUCLEIC ACID MOLECULES AND PROTEINS AND USES THEREFOR

Box No. II APPLICANT

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)

The Wistar Institute of Anatomy and Biology
3601 Spruce Street
Philadelphia, Pennsylvania 19104
US

☐ This person is also inventor.

Telephone No.
215-898-0049

Facsimile No.
215-573-2456

Teleprinter No.

State (that is, country) of nationality:
US

State (that is, country) of residence:
US

This person is applicant for the purposes of: ☐ all designated States ☒ all designated States except the United States of America ☐ the United States of America only ☐ the States indicated in the Supplemental Box

Box No. III FURTHER APPLICANT(S) AND/OR (FURTHER) INVENTOR(S)

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)

Prendergast, George C.
414 Bryn Mawr Avenue
Bala-Cynwyd, Pennsylvania 19004
US

This person is:

☐ applicant only

☒ applicant and inventor

☐ inventor only (if this check-box is marked, do not fill in below.)

State (that is, country) of nationality:
US

State (that is, country) of residence:
US

This person is applicant for the purposes of: ☐ all designated States ☐ all designated States except the United States of America ☒ the United States of America only ☐ the States indicated in the Supplemental Box

☒ Further applicants and/or (further) inventors are indicated on a continuation sheet.

Box No. IV AGENT OR COMMON REPRESENTATIVE; OR ADDRESS FOR CORRESPONDENCE

The person identified below is hereby/has been appointed to act on behalf of the applicant(s) before the competent International Authorities as:

☒ agent ☐ common representative

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)

Bak, Mary E.
Howson and Howson
Spring House Corporate Center
P.O. Box 457
Spring House, Pennsylvania 19477
US

Telephone No.
215-540-9200

Facsimile No.
215-540-5818

Teleprinter No.

☐ Address for correspondence: Mark this check-box where no agent or common representative is/has been appointed and the space above is used instead to indicate a special address to which correspondence should be sent.

| Continuation of Box No. III FURTHER APPLICANT(S) AND/OR (FURTHER) INVENTOR(S) | |
|--|--|
| <i>If none of the following sub-boxes is used, this sheet should not be included in the request.</i> | |
| <p>Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)</p> <p>Ge, Kai 4427 Spruce Street Philadelphia, Pennsylvania 19104 US</p> | <p>This person is:</p> <p><input type="checkbox"/> applicant only</p> <p><input checked="" type="checkbox"/> applicant and inventor</p> <p><input type="checkbox"/> inventor only (If this check-box is marked, do not fill in below.)</p> |
| State (that is, country) of nationality: China | State (that is, country) of residence: US |
| <p>This person is applicant for the purposes of: <input type="checkbox"/> all designated States <input type="checkbox"/> all designated States except the United States of America <input checked="" type="checkbox"/> the United States of America only <input type="checkbox"/> the States indicated in the Supplemental Box</p> | |
| <p>Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)</p> | <p>This person is:</p> <p><input type="checkbox"/> applicant only</p> <p><input type="checkbox"/> applicant and inventor</p> <p><input type="checkbox"/> inventor only (If this check-box is marked, do not fill in below.)</p> |
| State (that is, country) of nationality: | State (that is, country) of residence: |
| <p>This person is applicant for the purposes of: <input type="checkbox"/> all designated States <input type="checkbox"/> all designated States except the United States of America <input type="checkbox"/> the United States of America only <input type="checkbox"/> the States indicated in the Supplemental Box</p> | |
| <p>Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)</p> | <p>This person is:</p> <p><input type="checkbox"/> applicant only</p> <p><input type="checkbox"/> applicant and inventor</p> <p><input type="checkbox"/> inventor only (If this check-box is marked, do not fill in below.)</p> |
| State (that is, country) of nationality: | State (that is, country) of residence: |
| <p>This person is applicant for the purposes of: <input type="checkbox"/> all designated States <input type="checkbox"/> all designated States except the United States of America <input type="checkbox"/> the United States of America only <input type="checkbox"/> the States indicated in the Supplemental Box</p> | |
| <p>Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)</p> | <p>This person is:</p> <p><input type="checkbox"/> applicant only</p> <p><input type="checkbox"/> applicant and inventor</p> <p><input type="checkbox"/> inventor only (If this check-box is marked, do not fill in below.)</p> |
| State (that is, country) of nationality: | State (that is, country) of residence: |
| <p>This person is applicant for the purposes of: <input type="checkbox"/> all designated States <input type="checkbox"/> all designated States except the United States of America <input type="checkbox"/> the United States of America only <input type="checkbox"/> the States indicated in the Supplemental Box</p> | |
| <p><input type="checkbox"/> Further applicants and/or (further) inventors are indicated on another continuation sheet.</p> | |

Box No.V DESIGNATION OF STATE

The following designations are hereby made under Rule 4.9(a) (mark the applicable check-boxes; at least one must be marked):

Regional Patent

- ☐ **AP** ARIPO Patent: GH Ghana, GM Gambia, KE Kenya, LS Lesotho, MW Malawi, SD Sudan, SL Sierra Leone, SZ Swaziland, TZ United Republic of Tanzania, UG Uganda, ZW Zimbabwe, and any other State which is a Contracting State of the Harare Protocol and of the PCT
- ☐ **EA** Eurasian Patent: AM Armenia, AZ Azerbaijan, BY Belarus, KG Kyrgyzstan, KZ Kazakhstan, MD Republic of Moldova, RU Russian Federation, TJ Tajikistan, TM Turkmenistan, and any other State which is a Contracting State of the Eurasian Patent Convention and of the PCT
- ☒ **EP** European Patent: AT Austria, BE Belgium, CH and LI Switzerland and Liechtenstein, CY Cyprus, DE Germany, DK Denmark, ES Spain, FI Finland, FR France, GB United Kingdom, GR Greece, IE Ireland, IT Italy, LU Luxembourg, MC Monaco, NL Netherlands, PT Portugal, SE Sweden, and any other State which is a Contracting State of the European Patent Convention and of the PCT
- ☐ **OA** OAPI Patent: BF Burkina Faso, BJ Benin, CF Central African Republic, CG Congo, CI Côte d'Ivoire, CM Cameroon, GA Gabon, GN Guinea, GW Guinea-Bissau, ML Mali, MR Mauritania, NE Niger, SN Senegal, TD Chad, TG Togo, and any other State which is a member State of OAPI and a Contracting State of the PCT (if other kind of protection or treatment desired, specify on dotted line)

National Patent (if other kind of protection or treatment desired, specify on dotted line):

- | | |
|--|--|
| <input type="checkbox"/> AE United Arab Emirates | <input type="checkbox"/> LR Liberia |
| <input type="checkbox"/> AL Albania | <input type="checkbox"/> LS Lesotho |
| <input type="checkbox"/> AM Armenia | <input type="checkbox"/> LT Lithuania |
| <input type="checkbox"/> AT Austria | <input type="checkbox"/> LU Luxembourg |
| <input checked="" type="checkbox"/> AU Australia | <input type="checkbox"/> LV Latvia |
| <input type="checkbox"/> AZ Azerbaijan | <input type="checkbox"/> MA Morocco |
| <input type="checkbox"/> BA Bosnia and Herzegovina | <input type="checkbox"/> MD Republic of Moldova |
| <input type="checkbox"/> BB Barbados | <input type="checkbox"/> MG Madagascar |
| <input type="checkbox"/> BG Bulgaria | <input type="checkbox"/> MK The former Yugoslav Republic of Macedonia |
| <input type="checkbox"/> BR Brazil | <input type="checkbox"/> MN Mongolia |
| <input type="checkbox"/> BY Belarus | <input type="checkbox"/> MW Malawi |
| <input checked="" type="checkbox"/> CA Canada | <input type="checkbox"/> MX Mexico |
| <input type="checkbox"/> CH and LI Switzerland and Liechtenstein | <input type="checkbox"/> NO Norway |
| <input type="checkbox"/> CN China | <input type="checkbox"/> NZ New Zealand |
| <input type="checkbox"/> CR Costa Rica | <input type="checkbox"/> PL Poland |
| <input type="checkbox"/> CU Cuba | <input type="checkbox"/> PT Portugal |
| <input type="checkbox"/> CZ Czech Republic | <input type="checkbox"/> RO Romania |
| <input type="checkbox"/> DE Germany | <input type="checkbox"/> RU Russian Federation |
| <input type="checkbox"/> DK Denmark | <input type="checkbox"/> SD Sudan |
| <input type="checkbox"/> DM Dominica | <input type="checkbox"/> SE Sweden |
| <input type="checkbox"/> EE Estonia | <input type="checkbox"/> SG Singapore |
| <input type="checkbox"/> ES Spain | <input type="checkbox"/> SI Slovenia |
| <input type="checkbox"/> FI Finland | <input type="checkbox"/> SK Slovakia |
| <input type="checkbox"/> GB United Kingdom | <input type="checkbox"/> SL Sierra Leone |
| <input type="checkbox"/> GD Grenada | <input type="checkbox"/> TJ Tajikistan |
| <input type="checkbox"/> GE Georgia | <input type="checkbox"/> TM Turkmenistan |
| <input type="checkbox"/> GH Ghana | <input type="checkbox"/> TR Turkey |
| <input type="checkbox"/> GM Gambia | <input type="checkbox"/> TT Trinidad and Tobago |
| <input type="checkbox"/> HR Croatia | <input type="checkbox"/> TZ United Republic of Tanzania |
| <input type="checkbox"/> HU Hungary | <input type="checkbox"/> UA Ukraine |
| <input type="checkbox"/> ID Indonesia | <input type="checkbox"/> UG Uganda |
| <input type="checkbox"/> IL Israel | <input checked="" type="checkbox"/> US United States of America |
| <input type="checkbox"/> IN India | <input type="checkbox"/> UZ Uzbekistan |
| <input type="checkbox"/> IS Iceland | <input type="checkbox"/> VN Viet Nam |
| <input checked="" type="checkbox"/> JP Japan | <input type="checkbox"/> YU Yugoslavia |
| <input type="checkbox"/> KE Kenya | <input type="checkbox"/> ZA South Africa |
| <input type="checkbox"/> KG Kyrgyzstan | <input type="checkbox"/> ZW Zimbabwe |
| <input type="checkbox"/> KP Democratic People's Republic of Korea | |
| <input type="checkbox"/> KR Republic of Korea | |
| <input type="checkbox"/> KZ Kazakhstan | |
| <input type="checkbox"/> LC Saint Lucia | |
| <input type="checkbox"/> LK Sri Lanka | |

Check-boxes reserved for designating States which have become party to the PCT after issuance of this sheet:

Precautionary Designation Statement: In addition to the designations made above, the applicant also makes under Rule 4.9(b) all other designations which would be permitted under the PCT except any designation(s) indicated in the Supplemental Box as being excluded from the scope of this statement. The applicant declares that those additional designations are subject to confirmation and that any designation which is not confirmed before the expiration of 15 months from the priority date is to be regarded as withdrawn by the applicant at the expiration of that time limit. (Confirmation (including fees) must reach the receiving Office within the 15-month time limit.)

Supplemental Box *If the Supplemental Box is not used, this sheet should not be included in the request.*

1. If, in any of the Boxes, the space is insufficient to furnish all the information: in such case, write "Continuation of Box No. ..." [indicate the number of the Box] and furnish the information in the same manner as required according to the captions of the Box in which the space was insufficient, in particular:

- (i) if more than two persons are involved as applicants and/or inventors and no "continuation sheet" is available: in such case, write "Continuation of Box No. III" and indicate for each additional person the same type of information as required in Box No. III. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below;
- (ii) if, in Box No. II or in any of the sub-boxes of Box No. III, the indication "the States indicated in the Supplemental Box" is checked: in such case, write "Continuation of Box No. II" or "Continuation of Box No. III" or "Continuation of Boxes No. II and No. III" (as the case may be), indicate the name of the applicant(s) involved and, next to (each) such name, the State(s) (and/or, where applicable, ARIPO, Eurasian, European or OAPI patent) for the purposes of which the named person is applicant;
- (iii) if, in Box No. II or in any of the sub-boxes of Box No. III, the inventor or the inventor/applicant is not inventor for the purposes of all designated States or for the purposes of the United States of America: in such case, write "Continuation of Box No. II" or "Continuation of Box No. III" or "Continuation of Boxes No. II and No. III" (as the case may be), indicate the name of the inventor(s) and, next to (each) such name, the State(s) (and/or, where applicable, ARIPO, Eurasian, European or OAPI patent) for the purposes of which the named person is inventor;
- (iv) if, in addition to the agent(s) indicated in Box No. IV, there are further agents: in such case, write "Continuation of Box No. IV" and indicate for each further agent the same type of information as required in Box No. IV;
- (v) if, in Box No. V, the name of any State (or OAPI) is accompanied by the indication "patent of addition," or "certificate of addition," or if, in Box No. V, the name of the United States of America is accompanied by an indication "continuation" or "continuation-in-part": in such case, write "Continuation of Box No. V" and the name of each State involved (or OAPI), and after the name of each such State (or OAPI), the number of the parent title or parent application and the date of grant of the parent title or filing of the parent application;
- (vi) if, in Box No. VI, there are more than three earlier applications whose priority is claimed: in such case, write "Continuation of Box No. VI" and indicate for each additional earlier application the same type of information as required in Box No. VI;
- (vii) if, in Box No. VI, the earlier application is an ARIPO application: in such case, write "Continuation of Box No. VI", specify the number of the item corresponding to that earlier application and indicate at least one country party to the Paris Convention for the Protection of Industrial Property or one Member of the World Trade Organization for which that earlier application was filed.

2. If, with regard to the precautionary designation statement contained in Box No. V, the applicant wishes to exclude any State(s) from the scope of that statement: in such case, write "Designation(s) excluded from precautionary designation statement" and indicate the name or two-letter code of each State so excluded.

3. If the applicant claims, in respect of any designated Office, the benefits of provisions of the national law concerning non-prejudicial disclosures or exceptions to lack of novelty: in such case, write "Statement concerning non-prejudicial disclosures or exceptions to lack of novelty" and furnish that statement below.

"Continuation of Box No. IV"

Kita, Stanley B.
Smith, George A.
Kodroff, Cathy A.
Bak, William

All above attorneys are members of the firm of Howson and Howson.
Address of all is indicated in Box IV.

| Box No. VI PRIORITY CLAIM | | <input type="checkbox"/> Further priority claims are indicated in the Supplemental Box. | | |
|---|-------------------------------|---|---------------------------------------|---|
| Filing date of earlier application (day/month/year) | Number of earlier application | Where earlier application is: | | |
| | | national application: country | regional application: regional Office | international application: receiving Office |
| item (1) 31 August 1999 | 60/151,554 | US | | |
| item (2) | | | | |
| item (3) | | | | |

☒ The receiving Office is requested to prepare and transmit to the International Bureau a certified copy of the earlier application(s) (only if the earlier application was filed with the Office which for the purposes of the present international application is the receiving Office) identified above as item(s): (1)

* Where the earlier application is an ARIPO application, it is mandatory to indicate in the Supplemental Box at least one country party to the Paris Convention for the Protection of Industrial Property for which that earlier application was filed (Rule 4.10(b)(ii)). See Supplemental Box.

Box No. VII INTERNATIONAL SEARCHING AUTHORITY

Choice of International Searching Authority (ISA) (if two or more International Searching Authorities are competent to carry out the international search, indicate the Authority chosen; the two-letter code may be used):

ISA / US

Request to use results of earlier search; reference to that search (if an earlier search has been carried out by or requested from the International Searching Authority):

Date (day/month/year)

Number

Country (or regional Office)

Box No. VIII CHECK LIST; LANGUAGE OF FILING

This international application contains the following number of sheets:

request : 5

description (excluding sequence listing part) : 39

claims : 5

abstract : 1

drawings : 8

sequence listing part of description : 9

Total number of sheets : 67

This international application is accompanied by the item(s) marked below:

1. ☒ fee calculation sheet2. ☐ separate signed power of attorney3. ☒ copy of general power of attorney; reference number, if any:4. ☐ statement explaining lack of signature5. ☐ priority document(s) identified in Box No. VI as item(s):6. ☐ translation of international application into (language):7. ☐ separate indications concerning deposited microorganism or other biological material8. ☒ nucleotide and/or amino acid sequence listing in computer readable form9. ☒ other (specify): transmittal letter to USRO

Figure of the drawings which should accompany the abstract:

Language of filing of the international application: English

Box No. IX SIGNATURE OF APPLICANT OR AGENT

Next to each signature, indicate the name of the person signing and the capacity in which the person signs (if such capacity is not obvious from reading the request).

By:

Mary E. Bak
Mary E. Bak
Attorney for Applicants

| | | |
|---|--|--|
| For receiving Office use only | | 2. Drawings: <input type="checkbox"/> received: <input type="checkbox"/> not received: |
| 1. Date of actual receipt of the purported international application: | | |
| 3. Corrected date of actual receipt due to later but timely received papers or drawings completing the purported international application: | | |
| 4. Date of timely receipt of the required corrections under PCT Article 11(2): | | |
| 5. International Searching Authority (if two or more are competent): ISA / | 6. <input type="checkbox"/> Transmittal of search copy delayed until search fee is paid. | |

| |
|---|
| For International Bureau use only |
| Date of receipt of the record copy by the International Bureau: |

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
8 March 2001 (08.03.2001)

PCT

(10) International Publication Number
WO 01/16158 A3

(51) International Patent Classification?: **C12P 21/06**,
C07H 21/04, C12N 5/00, 1/20, 15/09, 15/63, A61K 38/00,
C07K 1/00

George, C. [US/US]; 414 Bryn Mawr Avenue, Bala-Cyn-
wyd, PA 19004 (US). GE, Kai [CN/US]; 4427 Spruce
Street, Philadelphia, PA 19104 (US).

(21) International Application Number: PCT/US00/23723

(74) Agents: **BAK, Mary, E.** et al.; Howson and Howson,
Spring House Corporate Center, P.O. Box 457, Spring
House, PA 19477 (US).

(22) International Filing Date: 30 August 2000 (30.08.2000)

(25) Filing Language: English

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(26) Publication Language: English

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NL, PT, SE).

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Published:
— With international search report.

(71) Applicant (*for all designated States except US*): **THE
WISTAR INSTITUTE OF ANATOMY AND BIOL-
OGY** [US/US]; 3601 Spruce Street, Philadelphia, PA
19104 (US).

(88) Date of publication of the international search report:
7 June 2001

(72) Inventors; and

(75) Inventors/Applicants (*for US only*): **PRENDERGAST,**

*For two-letter codes and other abbreviations, refer to the "Guid-
ance Notes on Codes and Abbreviations" appearing at the begin-
ning of each regular issue of the PCT Gazette.*



WO 01/16158 A3

(54) Title: BRIDGING INTEGRATOR-2 (BIN2) NUCLEIC ACID MOLECULES AND PROTEINS AND USES THEREFOR

(57) Abstract: The present invention provides Bin2 sequences and proteins encoded thereby. Also provided are compositions and methods utilizing these sequences and proteins in the diagnosis and treatment of blood disorders, including hepatocarcinoma. Further provided are oligonucleotides derived from sequences encoding Bin2, as well as compositions and methods utilizing same for diagnostic and therapeutic purposes.

INTERNATIONAL SEARCH REPORT

 International application No.
PCT/US00/23723

| A. CLASSIFICATION OF SUBJECT MATTER IPC(7) : Please See Extra Sheet. US CL : 435/69.1, 325, 252.3, 320.1; 536/23.1, 23.5; 530/300, 350 According to International Patent Classification (IPC) or to both national classification and IPC | | | | |
|---|--|---|---|--|
| B. FIELDS SEARCHED Minimum documentation searched (classification system followed by classification symbols) U.S. : 435/69.1, 325, 252.3, 320.1; 536/23.1, 23.5; 530/300, 350 Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) Please See Extra Sheet. | | | | |
| C. DOCUMENTS CONSIDERED TO BE RELEVANT | | | | |
| Category* | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. | | |
| X | US 5,605,830 A (PRENDERGAST ET AL.) 25 FEBRUARY 1997, See SEQ ID NO : 4 (res 136-153) matches Applicants' SEQ ID NO : 2 (res 138-155). | 2-4, 8 & 22 | | |
| A, P | US 5,958,753 A (PRENDERGAST) 28 SEPTEMBER 1999, see the entire document. | 1-9, 14 & 22 | | |
| <input type="checkbox"/> Further documents are listed in the continuation of Box C. <input type="checkbox"/> See patent family annex. | | | | |
| <table border="0"> <tr> <td> * Special categories of cited documents: "A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier document published on or after the international filing date "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "O" document referring to an oral disclosure, use, exhibition or other means "P" document published prior to the international filing date but later than the priority date claimed </td> <td> "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art "&" document member of the same patent family </td> </tr> </table> | | | * Special categories of cited documents: "A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier document published on or after the international filing date "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "O" document referring to an oral disclosure, use, exhibition or other means "P" document published prior to the international filing date but later than the priority date claimed | "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art "&" document member of the same patent family |
| * Special categories of cited documents: "A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier document published on or after the international filing date "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "O" document referring to an oral disclosure, use, exhibition or other means "P" document published prior to the international filing date but later than the priority date claimed | "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art "&" document member of the same patent family | | | |
| Date of the actual completion of the international search 29 NOVEMBER 2000 | | Date of mailing of the international search report 26 FEB 2001 | | |
| Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230 | | Authorized officer TEKCHAND SAIDHA Telephone No. (703) 308-0196 TERRY J. DEY PARALEGAL SPECIALIST TECHNOLOGY CENTER 1600 | | |

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US00/23723

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☒ Claims Nos.: 10,11, 12, 15, 17 & 20
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

Please See Extra Sheet.

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
1-9, 14 & 22

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
☐ No protest accompanied the payment of additional search fees.

A. CLASSIFICATION OF SUBJECT MATTER:

IPC (7):

C12P 21/06; C07H 21/04; C12N 5/00, 1/20, 15/09, 15/63; A61K 38/00; C07K 1/00

B. FIELDS SEARCHED

Electronic data bases consulted (Name of data base and where practicable terms used):

West search terms included : bin-1, bin-2, bridging integrator-2, BAR protein, C-MYC protein, etc. Stn files including - Caplus, Medline, Embase, Biosis & Biotechds. Sequence searches for the claimed SEQ ID NOs. in GenBank and protein data bases.

BOX II. OBSERVATIONS WHERE UNITY OF INVENTION WAS LACKING

This ISA found multiple inventions as follows:

This application contains the following inventions or groups of inventions which are not so linked as to form a single inventive concept under PCT Rule 13.1. In order for all inventions to be searched, the appropriate additional search fees must be paid.

Group I, claim(s) 1-9, 14 & 22, drawn to Bin2 protein, nucleic acid encoding Bin2 protein, vector, host cell, a diagnostic reagent and composition comprising the Bin2 protein.

Group II, claim(s) 13, drawn to a method of diagnosing hepatocarcinoma.

Group III, claim(s) 16, 18-19 & 21, drawn to anti Bin2 antibody, method and a kit:

Group IV, claim(s) 23-24, drawn to a method of detecting inappropriate expression of Box-depenedent myc-interacting protein-2 (Bin2).

Group V, claim(s) 25-27, drawn to a method of identifying compounds which inhibit binding of Bin2.

The inventions listed as Groups I-V do not relate to a single inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: Group I has a special technical feature of the nucleotide sequence encoding Bin2 protein, which Groups II-V do not share; Group II has a special technical feature of amplifying a DNA for diagnostics, which Groups I & III-V do not share; Group III has a special technical feature of an antibody, which Groups I-II & IV-V do not share; Group IV has a special technical feature of detecting inappropriate expression using nucleic acid, which Groups I-III & V do not share. Thus the various groups discussed above show a lack of unity of invention.